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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,967	10/16/2006	Rakesh Kumar	PR60682USW	7447

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EXAMINER	
PAGONAKIS, ANNA	
ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
05/21/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/599,967	**Applicant(s)** KUMAR ET AL.	
	Examiner ANNA PAGONAKIS	**Art Unit** 1614	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED _____ FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *06 January 2009*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *15-17 and 25*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Patricia A. Duffy/
Primary Examiner, Art Unit 1645

Continuation of 11. does NOT place the application in condition for allowance because:

Applicant's remarks presented in the after-final amendment regarding the 112 and 103 rejections has been considered and entered into the record, but are not persuasive.

With regard to Applicant's traversal of the 112 rejeciton stating that Applicant's contrued the rejection to be drawn solely to physiologically functional derivatives is unpersuasive. The record clearly states that the use of the word solvates is unclear, see page 2 of the Office Action mailed on 10/6/2008. Further, Applicant states that the specification provides guidance regarding the meaning of this term as well as examples of solvents that may be used to create such solvates. This is unpersuasive. Firstly, the rejection states "it is not clear from the claim language whether the compounds are corresponding to the structure of the instantly claimed solvates… or to the function is unclear." The rejections clearly states that structures nor functions of possible solvate compounds have been disclosed. Though the specification defines what is commonly known in the art as the definition of solvates and solvents known to create possible solvates, the disclosure still fails to teach actual structures or functions of solvates.

With regard to the 103 rejection, Applicant traverses stating that the therapeutic effects of a particular combination cannot be predicted a priori. Applicant further alleges that evidence has been presented that the benefits of any particular cancer treatment combination is unpredictable and that in some instances combination therapy offers no advantage in comparison with monotherapy with the single agents comprising the combination. This is not persuasive. It is common in the pharmaceutical art to combine agents to achieve maximum therapeutic efficacy with a reasonable expectation of success. In re Kerkhoven. Further, a reasoanble expectation of success is present because the combination of different agetns would be expected to have additive is not superadditive effects over one agent alone. Applicant further states that patients treated with the combination showed an improved rate of progression-free survival during treated compared with lapatinib monotherapy. In order to superadditive or superior results to be concluded, each agent must be administered at the same dosage and then the combination of the two compared to the inhibition demonstrated by each individual agent such that superadditive or superior results can in fact be concluded. In the instant case, Applicant has tested dramatically different dosages (i.e. 1000 mg lapatinib and 400 mg of Formula I) and further has compared this combination with lapatinib monotherapy alone and not monotherpay of Formula I, respectively. Applicant is reminded that evidence asserted to establish differences and/or unobvious results sufficient to dissipate a prima facie case of obviousness, there is a burden on the patent applicant to establish differences and/or unobvious results sufficient to dissipate a prima facie case of obviousness, there is a burden on the patent applicant to establish not only that the differences in results achieved are in fact "unexpected and unobvious" but also to establish that the differences are of practical signficance. See 27 USPQ2d Ex parte C 1492 (see page 1497, column 1, paragraph 4). A showing of unobviousness must be commensurace in scope with the claims which the evidence is offered to support.

The rejections are maintained for the reasons set forth above and those made previously of record.